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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,449	10/31/2003	Karla M. Robotti	10030218-1	2836

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EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 04/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,449	ROBOTTI, KARLA M.	
	Examiner	Art Unit	
	Marcela M. Cordero Garcia	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I, claims 1-23 in their reply filed on April 22, 2005 response is acknowledged.

In addition, Applicant elects in their reply of January 6, 2006, the species wherein the nucleophile is an amine moiety, wherein the linker includes a photocleavable group having the structure (IV), wherein the deglycosylated protein is released from the solid support by exposing the resin bound deglycosylated protein to light, and wherein the released proteins are subjected to mass spectrometric analysis. Claims 1-11 and 14-19 are readable thereon.

Claims 1-11 and 14-19 are presented for examination on the merits as they read upon the elected species.

Claims 1-11 and 14-19 have been searched and examined and found free of the prior art with respect to Applicant's elected species (however, please see 112 1st rejection below). Please note that no claims are written in independent form and thereofore, as drafted, the claims are not allowable.

Examiner elected a new species, wherein the nucleophile is a thiol moiety.

Claims 1-9 and 11 are readable upon the elected species and are presented for examination on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)).

Nature of the invention. The claims are drawn to a separation method of glycosylated and unglycosylated proteins.

State of the prior art. At the time the invention was made, it was noted by Wells et al. (Molecular and Cellular Proteomics, 2002) that "some of O-GlcNAc-modified residues are more resistant to β-elimination (e.g., O-GlcNAc-Thr followed by a Pro)". In addition, as reviewed by Spiro, "a strikingly large number of diverse carbohydrate-peptide linkages exist in nature". (Spiro, Glycobiology, 2002. Page 52R, column 1, lines 39-56).

Breadth of the claims. The claims are extremely broad, encompassing separation of any kind of glycosylated protein from deglycosylated ones. This would include any O-glycosylated proteins, N-glycosylated proteins, C-mannosylated, phosphoglycosylated, glypiated and mixtures thereof (See, e.g., Spiro, pages 43-47R, Tables I and II).

Working examples. One working example is disclosed in the specification, but the nature of the mixture of glycosylated / unglycosylated peptides is not disclosed.

Guidance in the specification. The specification provides little guidance regarding practice of the claimed methods. The specification refers generally to glycosylated proteins as compounds having a glycosyl group covalently bound to a protein (e.g., page 5, line 11-12) and does not distinguish from O-glycosylation to N-glycosylation, which are known to have distinct chemistries such as N-linked glycosylation to the amine nitrogen of asparagines side chains and O-linked glycosylation to the hydroxyl oxygen of serine and threonine chains. The instantly claimed method therefore, relies upon β -elimination (see, disclosure, page 19, lines 3-14) protocols, which is not always routinely obtainable by those skilled in the art as noted by Wells et al. (see above). There is no specific guidance regarding how the various types of glycosylation types and their different chemistries would be addressed. The specification does not disclose the glycopeptides used in the instantly claimed separation.

Predictability of the art. The glycopeptide art in general is acknowledged to be unpredictable (MPEP 2164.03). Spiro says: "A chronological survey of description of new glycopeptide linkages suggests that this stream of discoveries will continue for some time into the future. Indeed the finding in a variety of proteins of mannose linked by a C-C bond to the indole ring of Trp indicates that protein glycosylation does not even require an amino acid functional group and thereby expands the scope of future investigations into novel bonds." (page 52R, column 1, last paragraph and column 2).

Amount of experimentation necessary. Besides the general expectation that finding all types of glycopeptide linkages will require years of further research (Spiro,

page 52R), it would require extensive research to understand the fundamental chemistry of all types of glycopeptide linkages and their chemistries with regards to the instantly claimed method. Applicants have identified an interesting method which might be useful in some instances of glycopeptidation, but essentially all of the work required to ultimately develop a generic separation method for any kind of glycopeptide has been left for others.

For the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wells et al. (Molecular and Cellular Proteomics, 2002).

Wells et al. teach a method comprising:

a) obtaining a mixture comprising a glycosylated protein and unglycosylated proteins, wherein the glycosylated protein comprises a protein having a glycosylation

site and a glycosyl group bound to the protein via the glycosylation site (See, e.g., page 792, column 2, Figure 4).

b) contacting the mixture with a resin, wherein the resin comprises a nucleophile bound to a solid support via a linker (e.g., a thiol resin, page 793, column 1, lines 27-29), said contacting done under conditions sufficient to remove the glycosyl group from the glycosylated protein to yield a deglycosylated protein having a deglycosylation site (see, e.g., page 793, column 1, lines 18-20, and Figure 2), the deglycosylated protein bound to the solid support via the deglycosylated site; (See, e.g., page 795, column 2, lines 9-17, Figure 4). Please note that the deglycosylated site was further reacted with DTT by Wells et al., however, it still would read upon a "deglycosylated site" (see, e.g., disclosure, page 5, lines 18-19, which define deglycosylation site as the site from which the glycosyl group was removed from the protein, and page 19, lines 3-14 describing the step herein).

d) releasing the deglycosylated protein from the solid support. (See, e.g., page 793, column 1, lines 27-40; page 795, lines 9-17, Figure 4, Figure 7 and Table II).

Wells et al. do not expressly teach:

c) rinsing the bound deglycosylated protein, thereby removing unglycosylated proteins;

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Wells et al. by separating the glycosylated and unglycosylated peptides on the thiol column. The skilled artisan would have been

motivated to do so because Wells et al. shows unglycosylated proteins elute before thiol chromatography (page 799, Table II) and deglycosylated protein elutes after thiol chromatography (page 799, Table II) and because the thiol chromatography interacts only with the DTT modified peptides (i.e., originally glycosylated). There would have been a reasonable expectation of success, given the fact that the method was used on several samples, such as Synapsin I peptides, Lamin B receptor and nucleoporin Nup 155 as taught by Wells et al. (e.g., abstract, page 792). The adjustment of particular conventional working conditions (e.g., utilizing gel electrophoresis, HPLC or mass spectrometry on the eluted peptides, dephosphorylating the proteins prior to analysis within such analytical method) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan.

Thus, the invention as a whole is prima facie obvious over the reference, especially in the absence of evidence to the contrary. Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcela M. Cordero Garcia whose telephone number is (571) 272-2939. The examiner can normally be reached on M-Th 7:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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MMCG 01/06

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